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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,262	01/18/2002	Janice A. Brown	PC11044ADAM	1289

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EXAMINER	
DAVIS, DEBORAH A	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	10/053,262	BROWN ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) *4-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to the Office Action mailed November 20, 2003 is acknowledged. Currently, claims 1-3 are under consideration. Claim 1 has been amended and claims 4-11 has been withdrawn.

Information Disclosure Statement

2. The previous office action inadvertently stated that reference WO 00/23804 was not considered, it should have been reference JP081870 because no translation has been provided.

Correction/Clarification of Previous Office Action

3. Examiner inadvertently combined two form paragraphs in number six of the previous office action. The correct form paragraph rejection for claim 3 is under 35 U.S.C. 103(a) as being unpatentable over Cheung et al in view of Craig et al.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheung et al (A Scintillation Proximity Assay for Poly(ADP-ribose) Polymerase, Analytical Biochemistry, 2000, Vol. 282) in view of Schuurs et al (USP#4,016,043) and in further view of Metcalfe et al (USP#4,539,294).

Cheung et al teaches method to assay and measure the activity of PARP (see abstract). Cheung et al teaches a scintillation proximity assay (SPA) for evaluating PARP activity. PARP is contacted with NAD under conditions that allow PARP auto-ribosylation (see abstract). When the enzyme PARP is activated by DNA damage, it synthesizes Poly(ADP-ribose) (auto-ribosylation) activity from biotinylated NAD (see abstract). After PARP is auto-ribosylated, it is contacted with a detectable marker (see Figure 1.) The poly(ADP-ribose) is labeled with avidin-SPA beads (immobilized) and is excited by the scintillation (see Figure 1). Measuring the amount of PARP with a detectable marker is indicated of the amount of PARP (page 27, columns 1-2). Results indicated that PARP can use biotinylated NAD to synthesize poly(ADP-ribose) and can be used as a measurement of its enzyme activity (page 27, columns 1-2 and page 28, paragraph 2). PARP-SPA assay can also be adapted to a 96-well format for automatic high-throughput screening for PARP inhibitors (see abstract).

Cheung et al does not teach the exclusion of radioimmunoassay to detect PARP activity.

However, Schuurs et al teaches the disadvantages of using a radioimmunoassay in that although they are sensitive, the requirement of special equipment, trained staff, the need for extra safety measures to protect against and the short half-life span of the

radioactive labeling element. The possibility of replacing the radioactive label with an enzyme label is proposed (col. 1, lines 25-42).

Cheung et al does not teach immobilization of PARP.

However, Metcalfe et al teaches the advantage of immobilizing enzymes. Metcalfe et al discloses that the immobilization of enzymes on solid supports has advantages that have long been recognized. Metcalfe et al discloses that when enzymes are immobilized on a support and a measurement of its activity is made, the measurement corresponds to the active enzyme on that support rather than the total amount of enzyme immobilized. Inactive enzyme on the support not functioning as a catalyst, is commonly deposited during the immobilization process, and the sum of active and inactive enzyme corresponds to the total amount of enzyme deposited on the support (column 4, lines 61-68 and column 5, line 1).

It would have been obvious to one of ordinary skill in the art to want to modify the teaching of Cheung et al to exclude using a radioimmunoassay for extra safety measures when using radioactive products in a laboratory setting. Further, the exclusion of using radioactive products requires less disposal time; enzyme immunoassay provides a very simple and sensitive assay method. It would have been further obvious to immobilize the enzyme of PARP to get an accurate measurement of its enzymes that are active versus enzymes that are not (column 4, lines 61-68). Further, immobilization of reagents is well known in the art. A skilled artisan would recognize that immobilization is a well known modification of the prior art taught by Cheung et al that can be modified to include such a design choice.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cheung et al in view of Schuurs et al (USP#4,016,043) in further view of Metcalfe et al (USP#4,539,294) as applied to claims 1-2 and further in view of Craig et al (USP#6,465,199).

The teachings of Cheung, Schuurs and Metcalfe are set forth above and differ from the instant claim in not teaching that the method to assay PARP is conducted at 4 degrees C.

However, Craig et al teaches compositions and methods for monitoring enzymatic activity of several enzymes that includes Poly-ADP-ribose that is thought to play a fundamental role in cellular signaling (col. 25, lines 1-36) DNA repair and replication (col. 26, lines 39-45). Typically, measurements for these types of assays are performed at 0-37 degrees C. or may be performed at a higher temperature if that temperature is compatible with the enzyme under study (col. 37, lines 24-32).

It would have been obvious to one of ordinary skill in the art to modify the method of Cheung et al in view Metcalfe et al and further in view of Schuurs et al to include performing the assay at a temperature that would be compatible with the enzyme Poly

(ADP-ribose) as taught by Craig et al to prevent denaturing and to allow the study of kinetic activity (col. 37, lines 24-32).

Response to Arguments

8. Applicant's arguments filed November 20, 2003 have been fully considered but they are not persuasive.

Applicant argues that the reference of Cheung et al does not anticipate the instant claimed invention because immobilization of PARP is not taught. Applicant further argues that claim 1 has been amended to exclude the use of radioactivity as a means to detect PARP activity. This argument is acknowledged but not found persuasive in light of the new line of rejection 103(a) above. Although the reference of Cheung et al is silent with respect to immobilization, the abstract recites that the assay for PARP can be adapted to a 96-well format for automatic high-throughout screening. One of ordinary skill in the art would recognize that a 96-well format for high-throughput screening for PARP as taught by Cheung et al can be modified to include immobilization as an well known design choice. In addition, a new line of rejection to address the immobilization of PARP is discussed above.

Applicant argues that it is only after PARP autoribosylation that streptavidin-conjugated SPA beads are added to reaction mixture is not found persuasive because the abstract teaches that PARP is identified by a biotinylated NAD that satisfies the instant claim 1.

Applicant argues that the reference of Craig et al does not disclose or suggest that avidin-streptavidin reagents could be successfully used either alone or in combination with an immobilized PARP to measure PARP activity.

This argument is not found persuasive because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The reference of Craig et al is not relied upon for whether it teaches or suggest that avidin-streptavidin reagents could successfully be used, either alone or in combination with an immobilized PARP, but rather the Examiner relies on the reference of Craig et al for its teaching of enzyme assays such as PARP, that are performed at a temperature of 0-37 degrees, which are within the recited ranges of the instant claim 3, to prevent denaturing and to allow the study of kinetic activity (see col. 37, lines 24-32). Further, avidin-streptavidin reagents and the immobilization of PARP is taught and suggested by the references of Cheung et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah A. Davis
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February 18, 2003

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2/27/03